

## PATENT SPECIFICATION

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## COMPLETE SPECIFICATION

## Metal Complexes of Hydrazide-Hydrazones and process for producing the same

We, FARBENFABRIKEN BAYER AKTIEN-GESELLSCHAFT, a body corporate organised under the laws of Germany, of Leverkusen-Bayerwerk, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention comprises metal complexes of hydrazones of hydrazides of heterocyclic carboxylic acids, the metal of which is selected from the 4th period and the 2nd to the 8th groups of the Periodic system as defined below and a valence of which is bound to oxygen, together with procedure for producing such complexes.

It is known that the hydrazides of heterocyclic carboxylic acids and hydrazones prepared by the reaction of such hydrazides with aldehydes and ketones are of therapeutic significance and, in particular, that such derivatives of isonicotinic acid have been found to be effective for combating tuberculosis in humans and animals. It is further known that hydrazides are capable of forming complexes with heavy metals and that in forming such complexes the hydrazides exert a reducing effect on the complex-forming metals at elevated temperature. Copper complexes of hydrazones of isocyclic carboxylic acid hydrazides (Bun-Hoi, et al., Comptes Rendues des Seances de l'Academie des Sciences 235: 330, 1952) have been prepared but the reaction was found by them to be specific for copper only and the resulting copper complexes have only slight therapeutic usefulness.

We have now found that new and highly useful complexes are obtained when hydrazones of hydrazides of heterocyclic carboxylic acids are reacted with compounds of complex-forming metals of the 4th Period and the 2nd to 8th groups of the periodic system, as shown on pages 154—5 of "Inorganic and Theoretical Chemistry" by F. Sherwood [Price 3s. 6d.]

Taylor (1947 edition). The discovery that the above metal complexes can be formed with ease and have new and valuable properties was surprising in view of the data presented in the literature, particularly because it was entirely unpredictable that the above metal complexes would exercise high therapeutic effects since the prevailing view is that the action of isonicotinic acid hydrazide and other tuberculostatic substances is due to the fact that metal is deemed to be withdrawn from the enzymatic system of the tuberculosis bacilli.

It is therefore, surprising that our new metal complexes have excellent tuberculostatic and veterinary utility. Our new compounds furthermore, in many cases, represent a marked change in solubility characteristics and thus, in accordance with the invention, it is frequently possible to prepare easily applicable water-soluble metal complexes—e.g., iron complexes—from hydrazide-hydrazones of heterocyclic carboxylic acids which are water-insoluble as such.

Heterocyclic carboxylic acids are used as starting materials in preparing our new hydrazide-hydrazones, for example, nicotinic acid, isonicotinic acid, alkylisonicotinic acids, pyromucic acid, the various quinoline carboxylic acid isomers, thiophene carboxylic acid, pyrazole carboxylic acid and pyrimidine carboxylic acids. The heterocyclic carboxylic acids may, for example, be converted by way of their esters into the corresponding hydrazides and then reacted with any desired aliphatic, aromatic or heterocyclic aldehyde or ketone to produce the desired hydrazones. These hydrazide-hydrazones are reacted, according to this invention, with metallic compounds particularly metal salts, of complex forming metals of the 4th Period and the 2nd to 8th groups of the periodic system as defined. The hydrazide-hydrazone metal complexes so formed may be represented by the following type formula:

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